



Original article

[Translated article] Checklist for the pharmaceutical care of patients with interstitial lung disease (CheckEPID): A Delphi-based consensus

Marta Calvin-Lamas^{a,*}, Miguel Ángel Calleja Hernández^b, Emilio Monte-Boquet^c, Miguel Ángel Rodríguez Sagrado^d and Pere Ventayol Bosch^e

^a Servicio de Farmacia, Complejo Hospitalario Universitario A Coruña (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain

^b Servicio de Farmacia, Hospital Universitario Virgen Macarena, Sevilla, Spain

^c Servicio de Farmacia, Hospital Universitari i Politècnic La Fe, Valencia, Spain

^d Servicio de Farmacia, Hospital Universitario Ramón y Cajal, Madrid, Spain

^e Servicio de Farmacia Hospitalaria, Hospital Universitari Son Espases, Palma de Mallorca, Spain



ARTICLE INFO

Article history:

Received 20 April 2023

Accepted 14 June 2023

Available online 19 October 2023

Keywords:

Interstitial lung disease

Idiopathic pulmonary fibrosis

Antifibrotic agents

Nintedanib

Pirfenidone

Pharmaceutical care

Delphi technique

A B S T R A C T

Objective: To develop a checklist to facilitate pharmaceutical care for patients with interstitial lung disease who require or are undergoing treatment with antifibrotic drugs.

Method: Five hospital pharmacists developed an initial list of 37 items divided into 4 blocks: (1) First visit, which included general patient data and data from the first treatment; (2) follow-up visits, assessing aspects of the follow-up of the treatment with nintedanib or pirfenidone; (3) telepharmacy, consisting of the evaluation of the inclusion of patients in a program of this type, course of the disease, and identification of the contact with the pharmacy service; (4) non-pharmacological treatment and patient information. To decide its potential inclusion in the checklist, 2 rounds of the Delphi were carried out in which the panelists had to assess the degree of agreement of each proposed item according to its “utility”, which was the determining criterion for its inclusion, and its “applicability”.

Results: Forty-eight hospital pharmacists were contacted, 30 (63%) agreed in writing to participate, 28 (58%) completed the first round of the Delphi, and 27 (56%) completed the second round. After the first round of the Delphi, the questionnaire was amended and comprised 40 items. Of the 40 items evaluated after the 2 rounds of the Delphi, there were 2 that, based on utility, the participants did not reach consensus for inclusion in the checklist: the one referring to “History of surgical intervention, specifically abdominal surgery in the last 4 weeks” (finally kept on the checklist due to its involvement in the indication of nintedanib) and to make recommendations on “Relaxation”. No consensus was reached on their applicability for 2 of the items: “Patient stratification according to the Spanish Society of Hospital Pharmacy (SEFH) chronic patient model” and “Collection of Results Reported by the Patient”.

Conclusions: The management of patients with ILD and/or pulmonary fibrosis is complex and requires a multidisciplinary approach where the hospital pharmacist plays a key role, especially, although not only, in monitoring drug treatment. We believe that this checklist can contribute from pharmaceutical care to improving the integrated care of patients with ILD who require or are undergoing treatment with antifibrotic drugs.

© 2023 Sociedad Española de Farmacia Hospitalaria (S.E.F.H.). Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Lista de comprobación para la atención farmacéutica del paciente con enfermedad pulmonar intersticial (CheckEPID): un consenso basado en el método Delphi

R E S U M E N

Objetivo: desarrollar una lista de comprobación para facilitar la atención farmacéutica al paciente con enfermedad pulmonar intersticial que requieren o están en tratamiento con antifibróticos.

Método: cinco especialistas en farmacia hospitalaria desarrollaron un listado inicial de 37 ítems divididos en 4 bloques: 1) Primera visita del paciente, que incluía datos generales del paciente y datos del primer tratamiento;

Palabras clave:

Enfermedad pulmonar intersticial

fibrosis pulmonar idiopática

antifibróticos

nintedanib

DOI of original article: <https://doi.org/10.1016/j.farma.2023.06.010>.

* Corresponding author at: Complejo Hospitalario Universitario A Coruña, Servicio de Farmacia, As Xubias, 84, 15006 A Coruña Tfno: 981176479, Spain.

E-mail address: marta.calvin.lamas@sergas.es (M. Calvin-Lamas).

<https://doi.org/10.1016/j.farma.2023.09.004>

1130-6343/© 2023 Sociedad Española de Farmacia Hospitalaria (S.E.F.H.). Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

pirfenidona
atención farmacéutica
método Delphi

2) Visitas de seguimiento, valorando aspectos del seguimiento del tratamiento con nintedanib o pirfenidona; 3) Telefarmacia, consistente en la evaluación de la inclusión de pacientes en un programa de este tipo, evolución de la enfermedad, e identificación del contacto con el servicio de farmacia; 4) Tratamiento no farmacológico e información al paciente. Para decidir su potencial inclusión en el listado de comprobación se realizaron dos rondas del Delphi en las que los panelistas tenían que valorar de cada ítem propuesto su grado de acuerdo con su “utilidad”, que fue el criterio determinante para su inclusión, y su “aplicabilidad”.

Resultados: se contactó con 48 farmacéuticos hospitalarios, 30 (63%) aceptaron por escrito participar, 28 (58%) completaron la primera ronda del Delphi, y 27 (56%) completaron la segunda ronda. Después de la primera ronda el cuestionario se modificó y quedó constituido por 40 ítems. De los 40 ítems evaluados tras las dos rondas del Delphi, hubo dos que, basados en la utilidad, los participantes del Delphi no alcanzaron el consenso para su inclusión en el listado: el referido a “Antecedentes de intervención quirúrgica, específicamente cirugía abdominal en las últimas 4 semanas” (finalmente mantenido en el listado por su implicación en la indicación de nintedanib) y el de realizar recomendaciones sobre “Relajación”. En dos de los ítems no se alcanzó consenso sobre su aplicabilidad: “Estratificación del paciente según el modelo del paciente crónico de la SEFH” y “Recogida de Resultados Comunicados por el Paciente”.

Conclusiones: el manejo del paciente con EPI y/o fibrosis pulmonar es complejo y requiere una aproximación multidisciplinar donde el farmacéutico hospitalario juega un papel clave, en especial, aunque no solamente, en el seguimiento del tratamiento farmacológico. Creemos que esta lista de comprobación puede desde la atención farmacéutica contribuir a mejorar la atención integrada de los pacientes con EPI que requieren o están en tratamiento con antifibróticos.

© 2023 Sociedad Española de Farmacia Hospitalaria (S.E.F.H.). Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Interstitial lung diseases (ILDs) are a heterogeneous group of disorders characterized by inflammation and/or fibrosis of the pulmonary parenchyma.¹ Idiopathic interstitial pneumonias are the most common condition. Within this subset, idiopathic pulmonary fibrosis (IPF) has the highest prevalence² and is the quintessential example of fibrotic ILDs.³ In Spain, although the estimated number of patients with IPF is between 8000 and 12 000,⁴ its incidence is expected to increase due to improved diagnostic methods and population ageing.⁵ Idiopathic pulmonary fibrosis is characterized by progressive worsening of dyspnoea and lung function and has a poor prognosis,⁶ with a median survival without treatment of 2–5 years after diagnosis.^{2,7} In Spain, the leading cause of lung transplantations is ILD (42% of transplantations), ahead of emphysema/chronic obstructive pulmonary disease (35%).⁸

Among the unmet needs expressed by patients with IPF is the improvement of the multidisciplinary care required by this disease.⁹ A possible solution is provided by the World Health Organization's proposals regarding chronic conditions; it suggested the implementation of an integrated care model that covers the entire care continuum, from diagnosis until end-of-life, and caters to the patients' needs whilst being patient-centered.¹⁰ Hospital pharmacists play a crucial role in this integrated care model for patients with pulmonary fibrosis.¹¹ Their responsibilities include monitoring and educating patients about their treatment, polypharmacy, and, in general, rationalizing pharmacological treatment, advising on adverse reaction prevention and management, monitoring for potential interactions, improving medication adherence and physician follow-up, providing guidance on overcoming daily life challenges by steering patients toward patient care and support programs, and encouraging patients to actively participate in managing their disease.^{11–14}

The Spanish Society of Hospital Pharmacy (SEFH) has incorporated this integrated care model within its chronic patient care model¹⁵ and in its definition of pharmaceutical care.¹⁶ Within this framework, the objective of this project was as follows: a group of hospital pharmacists were tasked with the development of a checklist (CheckEPID) to facilitate pharmaceutical care for patients with diffuse interstitial lung disease (DILD) who require or are undergoing treatment with antifibrotics.

Materials and methods

Selection of experts and development of the proposed checklist

The project was coordinated by 2 hospital pharmacists of recognized standing with expertise in providing pharmaceutical care to patients with IPF. Together with 3 other experts, they formed the scientific committee responsible for establishing the objectives, design, scheduling, and criteria used to select the expert panel. The scientific committee received assistance from a consulting company specialising in research and methodology.

The scientific committee developed an initial list of questions to be evaluated by the expert panel. This list comprised 31 questions (with a total of 37 items) divided into 4 blocks, as follows: (1) First patient visit, which included general patient data: 12 questions on age, sex, race, weight, allergies, pulmonary, renal and hepatic function, history of surgical intervention, vaccination record, stratification according to the SEFH chronic patient model, collection of Patient-Reported Outcomes (PRO), and first treatment data (with 10 questions related to treatment with nintedanib or pirfenidone, the only currently approved treatments for IPD); (2) follow-up visits: 4 questions related to assessing aspects of nintedanib or pirfenidone treatment follow-up, adherence, and appropriateness of treatment; (3) telepharmacy: 3 questions on evaluating patients for their inclusion in a telepharmacy program, evolution of the disease, and identification of the person authorized for telepharmacy access; and (4) non-pharmacological treatment and patient information: 2 questions on hygiene and dietary recommendations and the elimination of toxic habits. Annex 1 contains details of the initial checklist (see Annex).

The scientific committee selected panellists to participate in the Delphi method on the basis of their expertise, type of hospital, and geographical distribution.

The Delphi method used in the project

A modified Delphi method was used in this study. Like other consensus techniques, the Delphi method seeks to achieve a general agreement or convergence of opinion on a particular topic, particularly those for which there is no evidence or any evidence is controversial. The Delphi method rests on 4 key features: anonymity, to prevent the dominance of certain opinions; iteration, to allow participants to change their

opinion; controlled feedback, showing the group and individual responses; and statistical analysis, to provide a summary measure that quantifies the degree of consensus.¹⁷ Together with other qualitative techniques, this method has already been used in other projects related to the management of IPD.^{18,19}

The consulting company contacted potential panellists via email with a brief explanation of the project, inviting them to participate, and, if so, to appear on the published list of participants.

Between March and June 2022, 2 rounds of Delphi were conducted using a specific web tool developed by the consulting company. For each questionnaire item, panellists had to rate 2 attributes for the potential inclusion of the item in the checklist: "usefulness", defined as "the suitability/relevance of the information or action mentioned for its inclusion in the checklist"; and "applicability", understood as "the feasibility of applying the information or action mentioned in typical pharmaceutical care practice taking into account typical practice in their center". Both attributes were scored on a 5-point Likert scale where the degree of agreement ranged from 1 (completely disagree) to 5 (completely agree). The second round only included items on which consensus had not been reached regarding their usefulness or applicability. In this second round, the panellists used the tool to view information on the group responses for each item (relative frequency distribution of responses on the Likert scale) and the individual responses from the first round.

Statistical analysis

Responses on the Likert scale were grouped into 3 categories: scores of 1 or 2 corresponded to "disagreement", 3 corresponded to "inconclusive", and 4 or 5 corresponded to "agreement". Consensus was deemed to have been reached when at least 70% of participants chose 1 of the 3 categories. However, to make the results more understandable, the level of consensus was graded into 4 categories: "unanimity" (100%), "strong consensus" (80%–99%), "consensus" (70%–79%), and "no consensus" (<70%).

The statistical analysis was primarily descriptive. The characteristics of the survey participants are shown with the absolute and relative frequency of each category of the variable presented. For each attribute of each item, we present the percentage of responses in each of the 3 agreement categories, the median Likert scale score as a summary measure of the level of agreement, and the level of consensus achieved. Statistical analysis was conducted using Microsoft Excel for Microsoft 365 MSO.

Results

Overall participation, participant characteristics, and overall consensus results

Forty-eight hospital pharmacists were contacted, of whom 30 (63%) agreed to participate, 28 (58%) completed the first round, and 27 (56%) completed the second round. More than half of the participants were from Catalonia, the Community of Madrid, and the Valencian Community. There was no representation from the Principality of Asturias, Castille and León, the Chartered Community of Navarre, La Rioja, and the autonomous cities of Ceuta and Melilla (Table 1). In total, 70% of the participants were from third-level hospitals, almost two-thirds had over 6 years' of experience, and nearly half had treated more than 20 patients with IPD and antifibrotic therapy in the past 12 months (Table 1).

In the first round, for the attribute usefulness, the expert panel reached unanimity on 8 items out of the 37, and strong consensus on 22; and for the attribute applicability, they reached unanimity on 3 items, strong consensus on 15, consensus on 6, and no consensus on 13. The scientific committee reviewed the results of the first round and modified the questionnaire. The vaccination item was divided into

Table 1

Characteristics of the Delphi participants.

| Characteristic | n = 28, (%) |
|---|-------------|
| <i>Autonomous Community</i> | |
| Andalusia | 2 (7) |
| The Balearic Islands | 2 (7) |
| Catalonia | 5 (18) |
| The Valencian Community | 5 (18) |
| Galicia | 2 (7) |
| Community of Madrid | 5 (18) |
| Others ^a | 6 (21) |
| <i>Level of hospital</i> | |
| Third level | 21 (71) |
| Second level | 5 (18) |
| First level | 2 (11) |
| <i>Number of patients with IPD and antifibrotic treatment in the last 12 months</i> | |
| More than 50 | 7 (25) |
| Between 21 and 50 | 6 (21) |
| Equal to or less than 20 | 15 (54) |
| <i>Years of experience</i> | |
| More than 6 y | 17 (61) |
| Between 3 and 5 y | 8 (28) |
| Equal or less than 2 y | 3 (11) |

^a Includes Aragon, the Canary Islands, Cantabria, Castile-La Mancha, Extremadura, and the Basque Country, with one participant each.

3 parts, one for each vaccination, and the wording of the item identifying the person authorized for telepharmacy access was modified. Annex 2 presents these inter-round modifications (see Annex).

The questionnaire now comprised 40 items. In the second round, for the attribute usefulness, the panel reached unanimity on 14 items, strong consensus on 23, consensus on 1, and no consensus on 2; and for the attribute applicability, they reached unanimity on 4 items, strong consensus on 26, consensus on 7, and no consensus on 3. Next, we present the detailed results of the second round.

Results of the second round of Delphi

All 12 demographic and clinical items under the heading "General patient data" (Table 2) had a median score of 4 or more on the attribute usefulness, although consensus was not reached on one of the items: "History of surgery, specifically abdominal surgery in the last 4 weeks, in the light of the specific recommendation in the nintedanib summary of product characteristics"; all items had a median score of 4 or more on the attribute applicability (Table 2), although consensus was not reached on 2 items: Patient stratification according to the SEFH chronic patient model was evaluated as "inconclusive" by 67% of participants; and the collection of PRO was evaluated as "inconclusive" by 52% and "agreement" by 44%.

In the block "First treatment", consensus was reached on all 10 items, which were unanimously deemed useful and applicable. Most of the items had a median of 5 (Table 2). However, regarding the item "How to measure PRO", the consensus on usefulness was "agree" (96% of responses), whereas the consensus on applicability was "inconclusive" (78% of responses; median = 3).

In the block "Follow-up visits", consensus was reached on all 7 items on the attributes usefulness and applicability (Table 2). All items had a median of 5, except for item "Include specific questions on adherence to treatment using the Morisky-Green-Levine scale", which had a median score of 4. The other adherence item "Include specific questions on adherence to treatment using dispensing records" had a median of 5.

There was consensus on the usefulness and applicability of all three "Telepharmacy" items, with median scores of 5 for usefulness and 4–5 for applicability (Table 2). In the "Non-pharmacological Treatment and Patient Information" block, consensus was not reached on the usefulness and applicability of the item "Recommendations on relaxation". In total, 59% of respondents agreed on its usefulness, and 37% agreed on its applicability. The remaining items had median scores of 4–5.

Table 2
Delphi results.

| | Round | Usefulness | | | | DC | Applicability | | | | | DC |
|---|-------|---------------|------------------|------------------|--------|----|---------------|------------------|----------------------|--------|----|----|
| | | Agreement (%) | Inconclusive (%) | Disagreement (%) | Median | | Agreement (%) | Inconclusive (%) | Disagreement (%) (%) | Median | | |
| First patient visit | | | | | | | | | | | | |
| General data | | | | | | | | | | | | |
| Age | 1 | 96 | 4 | 0 | 5 | SC | 100 | 0 | 0 | 5 | U | |
| Sex | 1 | 86 | 14 | 0 | 5 | SC | 89 | 7 | 4 | 5 | SC | |
| Weight | 1 | 93 | 7 | 0 | 5 | SC | 82 | 18 | 0 | 4 | SC | |
| Race | 2 | 81 | 19 | 0 | 4 | SC | 96 | 4 | 0 | 5 | SC | |
| Allergies, specifically to peanut and soybean | 2 | 93 | 7 | 0 | 5 | SC | 93 | 7 | 0 | 5 | SC | |
| Lung function before starting treatment (FVC, FEV1, FEV1/FVC, D _{LCO}) | 1 | 100 | 0 | 0 | 5 | U | 93 | 7 | 0 | 5 | SC | |
| Renal function test data before starting treatment | 1 | 86 | 14 | 0 | 5 | SC | 93 | 7 | 0 | 5 | SC | |
| Liver function test data before starting treatment | 1 | 96 | 4 | 0 | 5 | SC | 93 | 7 | 0 | 5 | SC | |
| History of surgical intervention, specifically abdominal surgery in the last 4 weeks | 2 | 67 | 33 | 0 | 4 | NC | 89 | 11 | 0 | 5 | SC | |
| Influenza vaccination record | 2 | 89 | 11 | 0 | 4 | SC | 78 | 15 | 7 | 4 | C | |
| Pneumococcal vaccination record | 2 | 93 | 7 | 0 | 4 | SC | 74 | 19 | 7 | 4 | C | |
| COVID-19 vaccination record | 2 | 93 | 7 | 0 | 4 | SC | 78 | 18 | 4 | 4 | C | |
| Patient stratification according to the SEFH Chronic Patient Model | 2 | 74 | 22 | 4 | 4 | C | 15 | 67 | 8 | 3 | NC | |
| Collection of PRO | 2 | 96 | 4 | 0 | 5 | SC | 44 | 52 | 4 | 3 | NC | |
| First treatment data | | | | | | | | | | | | |
| Report on expectations concerning the treatment of ILD | 2 | 100 | 0 | 0 | 5 | U | 85 | 15 | 0 | 5 | SC | |
| Provide information on nintedanib or pirfenidone dosing regimen | 1 | 96 | 4 | 0 | 5 | SC | 96 | 4 | 0 | 5 | SC | |
| Provide information on how to proceed in the event of forgetting to take a dose of medication | 1 | 96 | 4 | 0 | 5 | SC | 96 | 0 | 4 | 5 | SC | |
| Provide information on storage conditions of nintedanib or pirfenidone | 1 | 93 | 4 | 4 | 5 | SC | 96 | 0 | 4 | 5 | SC | |
| Provide information on the most frequent adverse reactions to nintedanib or pirfenidone | 1 | 100 | 0 | 0 | 5 | U | 100 | 0 | 0 | 5 | U | |
| Review the patient's complete pharmacological treatment, with special emphasis on drugs (or foods) with clinically relevant interactions with nintedanib or pirfenidone | 1 | 100 | 0 | 0 | 5 | U | 93 | 7 | 0 | 5 | SC | |
| Provide information on possible interactions of nintedanib or pirfenidone (St. John's wort and grapefruit juice) | 1 | 100 | 0 | 0 | 5 | U | 93 | 7 | 0 | 5 | SC | |
| How PRO are measured | 2 | 96 | 4 | 0 | 4 | SC | 22 | 78 | 0 | 3 | C | |
| Specific hygienic-dietary recommendations to patients on treatment with nintedanib or pirfenidone (especially on sun exposure for pirfenidone) | 1 | 96 | 4 | 0 | 5 | SC | 96 | 4 | 0 | 5 | SC | |
| Provide information on specific reliable sources (web pages and information materials on ILD, centre protocol information sheets, etc) | 2 | 100 | 0 | 0 | 4 | U | 70 | 30 | 0 | 4 | C | |
| Follow-up visit | | | | | | | | | | | | |
| Treatment with nintedanib: ask about current dosing regimen and intake in relation to food | 1 | 96 | 4 | 0 | 5 | SC | 89 | 11 | 0 | 5 | SC | |
| Treatment with pirfenidone: ask about follow-up of the initial ascending regimen, current dosing regimen, and intake in relation to food | 1 | 100 | 0 | 0 | 5 | U | 93 | 7 | 0 | 5 | SC | |
| Ask about the most frequent adverse effects caused by nintedanib (gastrointestinal disorders) or pirfenidone (photosensitivity and gastrointestinal disorders) | 1 | 100 | 0 | 0 | 5 | U | 100 | 0 | 0 | 5 | U | |
| Ask about interference with daily life caused by the most frequent adverse effects of treatment | 2 | 100 | 0 | 0 | 5 | U | 100 | 0 | 0 | 5 | U | |
| Ask about changes since the previous visit in terms of concomitant treatment with drugs or foods with potential interaction with pirfenidone or nintedanib | 1 | 100 | 0 | 0 | 5 | U | 96 | 4 | 0 | 5 | SC | |
| Assessment of adherence to treatment using the Morisky-Green-Levine scale | 2 | 89 | 11 | 0 | 5 | SC | 93 | 7 | 0 | 4 | SC | |
| Assessment of adherence to treatment using dispensing record | 1 | 82 | 18 | 0 | 5 | SC | 89 | 7 | 4 | 5 | SC | |

Table 2 (continued)

| | Round | Usefulness | | | | | Applicability | | | | |
|---|-------|---------------|------------------|------------------|--------|----|---------------|------------------|----------------------|--------|----|
| | | Agreement (%) | Inconclusive (%) | Disagreement (%) | Median | DC | Agreement (%) | Inconclusive (%) | Disagreement (%) (%) | Median | DC |
| <i>Telepharmacy</i> | | | | | | | | | | | |
| Evaluation of the patient's suitability for inclusion in a telepharmacy program | 2 | 100 | 0 | 0 | 5 | U | 89 | 11 | 0 | 4 | SC |
| Degree of evolution of IPD (degree of dyspnoea, need for oxygen therapy) | 2 | 100 | 0 | 0 | 5 | U | 93 | 7 | 0 | 4 | SC |
| Identification of the person authorized for contact in the telepharmacy service | 2 | 96 | 4 | 0 | 5 | SC | 81 | 19 | 0 | 5 | SC |
| <i>Non-pharmacological treatment and patient information</i> | | | | | | | | | | | |
| Recommendation on physical exercise | 2 | 96 | 4 | 0 | 4 | SC | 89 | 7 | 4 | 4 | SC |
| Recommendation on sleep habits | 2 | 93 | 7 | 0 | 4 | SC | 78 | 19 | 4 | 4 | C |
| Recommendation on relaxation habits | 2 | 59 | 37 | 4 | 4 | NC | 37 | 52 | 11 | 3 | NC |
| Recommendation on dietary habits | 2 | 100 | 0 | 0 | 5 | U | 93 | 4 | 4 | 4 | SC |
| Recommendation on the elimination of toxic habits, especially tobacco | 2 | 100 | 0 | 0 | 5 | U | 93 | 7 | 0 | 5 | SC |

NC, no consensus; C, consensus; SC, strong consensus; FVC, forced vital capacity; D_{LCO} , diffusing capacity for carbon monoxide; DILD, diffuse interstitial lung disease; FEV1, forced expiratory volume in 1 s; DC, degree of consensus; PRO, patient-reported outcomes; SEFH, Spanish Society of Hospital Pharmacy; U, unanimity.

Table 3

Checklist for the pharmaceutical care of patients with interstitial lung disease.

| | |
|---|---|
| First visit | |
| General data | Age Sex Weight Race Allergies, specifically to peanut and soybean Lung function before starting treatment (FVC, FEV1, FEV1/FVC, D_{LCO}) Renal function test data before starting treatment Liver function test data before starting treatment History of surgical intervention, specifically abdominal surgery in the last 4 weeks Influenza vaccination record Pneumococcal vaccination record COVID-19 vaccination record Patient stratification according to the SEFH Chronic Patient Model Collection of PRO (e.g., King's Brief Interstitial Lung Disease questionnaire ^a) ²¹ |
| First treatment | Report on expectations concerning the treatment of ILD Provide information on nintedanib or pirfenidone dosing regimen Provide information on how to proceed in the event of forgetting to take a dose of medication Provide information on storage conditions of nintedanib or pirfenidone Provide information on the most frequent adverse reactions to nintedanib or pirfenidone Review the patient's complete pharmacological treatment, with special emphasis on drugs (or foods) with clinically relevant interactions with nintedanib (potent inducers of P-glycoprotein involved in the metabolism of nintedanib, St. John's wort) or pirfenidone (tobacco, potent inducers of both CYP1A2 and other CYP isoenzymes involved in the metabolism of pirfenidone, grapefruit juice) Provide information on possible interactions of nintedanib or pirfenidone (St. John's wort and grapefruit juice) How to measure PRO ^b Specific hygienic-dietary recommendations to patients on treatment with nintedanib or pirfenidone (especially on sun exposure for pirfenidone) Provide information on specific reliable sources (web pages and informative materials on ILDs, centre protocol information sheets, etc) |
| Follow-up visits | Treatment with nintedanib: ask about current dosing regimen and intake in relation to food Treatment with pirfenidone: ask about follow-up of the initial ascending regimen, current dosing regimen, and intake in relation to food Ask about the most frequent adverse effects caused by nintedanib (gastrointestinal disorders) or pirfenidone (photosensitivity and gastrointestinal disorders) Ask about interference with daily life caused by the most frequent adverse effects of treatment Ask about changes since the previous visit in terms of concomitant treatment with drugs or foods with potential interaction with pirfenidone or nintedanib Assessment of adherence to treatment with the Morisky-Green-Levine scale ²² Assessment of adherence to treatment using dispensing record |
| Telepharmacy | Evaluation of the patient's suitability for inclusion in a telepharmacy program Degree of evolution of IPD (degree of dyspnoea, need for oxygen therapy) Identification of the person authorized for contact in the telepharmacy service |
| Non-pharmacological treatment and patient information (when deemed appropriate) | Recommendation on physical exercise Recommendation on sleep habits Recommendation on dietary habits Recommendation on the elimination of toxic habits, especially tobacco |

FVC, forced vital capacity; D_{LCO} , diffusing capacity for carbon monoxide; FEV1, forced expiratory volume in one second; DILD, diffuse interstitial lung disease; SEFH, Spanish Society of Hospital Pharmacy.

^a The King's Brief Interstitial Lung Disease questionnaire is a self-administered instrument for assessing health-related quality of life specific to interstitial lung disease. It comprises 15 items with 3 domains: psychological, dyspnoea and activities, and chest symptoms. A total score is obtained combining scores on the 3 domains.

^b Establish what should be measured, with what instrument, how often, and by whom, preferably in consensus with the hospital's multidisciplinary team.

Final checklist

After evaluating the results of the final Delphi round, the scientific committee decided to include in the checklist all items for which there was consensus on their usefulness. Initially, 2 items were excluded: the general data item "History of surgical intervention, specifically abdominal surgery in the last 4 weeks" and the non-pharmacological treatment item "Recommendations on relaxation". However, since treatment with nintedanib must be initiated at least 4 weeks after abdominal surgery,²⁰ the committee decided to retain this item. Table 3 presents the final checklist.

Discussion

The management of patients with ILD and/or pulmonary fibrosis is complex and requires a multidisciplinary approach in which hospital pharmacists play a crucial role, particularly, but not exclusively, in the monitoring of pharmacological treatment. The checklist we have developed is intended to help guide such monitoring as part of the pharmaceutical care of patients. It may be particularly useful for centers without a specialized unit for managing such patients.

There was no consensus on the usefulness of 2 items evaluated for inclusion in the list: the item "History of surgical intervention, specifically abdominal surgery in the last 4 weeks" and "Recommendation for relaxation". As mentioned above, the scientific committee decided to retain the former item on the list, given the implications of recent abdominal surgery on starting treatment with nintedanib. Regarding the item on relaxation, it should be noted that the chronic breathing difficulties, coughing, and fatigue experienced by these patients have a negative impact on their emotional wellbeing and quality of life by limiting their daily activities.^{23,24} Anxiety related to fear of these symptoms and the resulting loss of self-confidence can lead to increased disability and a dangerous vicious cycle.²³ Although research in this area is limited, stress control interventions may improve perceived stress and mood in patients with ILD.²³ The lack of consensus on the inclusion of such recommendations in the checklist may be due to limited research in this area or to hospital pharmacists lacking sufficient time and/or training to provide such recommendations. As a result, it is possible that other professionals in multidisciplinary teams caring for patients with ILD should be responsible for these types of interventions.

Although not decisive for their inclusion in the list, consensus was not reached on the applicability of 2 items: "Patient stratification according to the SEFH chronic patient model" and "Collection of PRO"; and consensus was inconclusive on the item "Method of measuring PRO". In 2012, the SEFH published a strategic plan for pharmaceutical care in chronic patients with the goal of enhancing their treatment. One of plan's objectives was "A patient-centered approach: stratification as a tool for the new care model".¹⁵ Specific stratification models have been published by the SEFH for human immunodeficiency virus infection,²⁵ immune-mediated inflammatory diseases,²⁶ and for patients with respiratory diseases in general,²⁷ but none has yet been developed that is specific to pulmonary fibrosis. This aspect may underlie the lack of consensus on this item regarding its applicability.

If our aim is to implement a patient-centered approach, we must deepen our understanding of how pulmonary fibrosis affects the patients' daily lives and identify the optimal methods to measure its impact. Nevertheless, there are very few PRO measures specifically designed for individuals with ILD or pulmonary fibrosis, and experience is very limited in those that have been developed or adapted for these patients.²⁸ Thus, we find it unsurprising that no consensus was reached regarding its applicability. However, it is also plausible that in this case, and in that of implementing a stratification model, pressure on healthcare services may have influenced its assessment in relation to its applicability.

A possible limitation of this project is the scarce participation of first- and second-level hospitals. In our setting, there is debate on whether these diseases should be treated in referral units (located in third-level hospitals) or if centers with a relevant patient volume can provide the needed level of specialization.²⁹ We believe that third-level hospitals are better placed to provide treatment due to the high volume of patients they treat for these diseases. Another possible limitation is that the attribute usefulness alone was the final criterion used to include items in the checklist. The reason for this decision lay in the definition participants received regarding "usefulness" ("the suitability/relevance of the information or action mentioned for its inclusion in the checklist"). However, it is relevant to note that for the checklist to be useful and generalizable to hospital pharmacy services that care for these patients, it must be applicable. Therefore, a field study should be conducted to assess the viability of this checklist in real-life conditions. Integrated patient support programs for IPF have demonstrated benefits for patients in terms of medication adherence.³⁰ Although the results are very preliminary, a retrospective study has shown that a patient-directed pharmacy program for IPF had a positive impact on adherence to antifibrotic treatment.³¹ It would be of interest to conduct a further study to evaluate the impact of using this checklist on antifibrotic treatment outcomes and patient satisfaction with care.

Overall, we believe that this checklist can complement previous initiatives²⁹ and, through pharmaceutical care, contribute to improving the integrated care of patients with ILD who require or are undergoing treatment with antifibrotics.

Ethical responsibilities

This is not a human research study, but rather a project to develop recommendations provided by an expert group. A systematic process (i.e., a modified Delphi method) was followed to obtain their opinions and reach a consensus on recommendations. Thus, given the nature of the project, it does not require mandatory approval from an Ethical Research Committee. The experts participated voluntarily and gave their written agreement to participate. Their responses are presented as an anonymized group.

Funding

The Delphi process that led to this Consensus Statement was facilitated by Ampersand Consulting, with the support and funding of Boehringer Ingelheim (BI). BI did not influence the opinions of the participating experts or the final consensus. The authors adhere to the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE) and did not receive any payment related to the development of this Consensus Statement. Dr. Fernando Rico-Villademoros, from COCIENTE S.L., provided editorial and writing support, which was contracted and funded by BI. BI had the opportunity to review the manuscript for accuracy from a medical and scientific standpoint, and in regard to potential intellectual property considerations.

Authorship

Marta Calvin Lamas and Miguel Ángel Calleja Hernández were responsible for the concept and design of the study. All authors were responsible for the intellectual content of the project, analysis and interpretation of the results, and preparation and revision of the manuscript. The final version of the manuscript was reviewed and approved by all authors, who consider themselves responsible for it. All authors met the authorship criteria outlined by the International Committee of Medical Journal Editors.

Responsibility and Rights Assignment

All authors accept their responsibility as defined by the International Committee of Medical Journal Editors (available at <http://www.icmje.org/>).

In the case of publication, the authors exclusively assign reproduction, distribution, translation, and public communication rights (through any audio, video, or electronic medium) of their work to *Farmacia Hospitalaria* and, by extension, to SEFH. For this purpose, a rights transfer letter will be signed upon submission of the manuscript through the online manuscript management system.

Contribution to the scientific literature

Among the unmet needs expressed by patients with interstitial lung disease is the improvement of multidisciplinary care required by this disease. To this end, it would be valuable to implement a patient-centered integrated care model that covers the entire care continuum and addresses all their needs. In such an integrated care model, hospital pharmacists would play a crucial role in the care of patients with pulmonary fibrosis.

The Spanish Society of Hospital Pharmacy (SEFH) has incorporated this integrated care model within its chronic patient care model and in its definition of pharmaceutical care. Overall, we believe that this checklist can complement previous initiatives and, from a pharmaceutical care perspective, contribute to improving the integrated care of patients with interstitial lung disease who require or are on antifibrotic therapy.

Conflicts of interest

Marta Calvin Lamas has received funding for scientific training, talks, or scientific advice from the following pharmaceutical companies: AstraZeneca, GlaxoSmithKline, CSL Behring, and Boehringer Ingelheim. Miguel Ángel Calleja Hernández has received funding for medical training, conference presentations, and research from the following pharmaceutical companies: Abbvie, Alexion, Almirall, Amgen, Astellas, AstraZeneca, Bayer, Biogen, Boehringer, Clovis, Genzyme, GSK, Grunenthal, Incyte, Janssen, Jazz, Kyowa, Lilly, Merck, MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, Seagen, Takeda, TEVA, UCB, and Viiv. Emilio Monte-Boquet has received honorariums or funding from various companies, such as Abbott/Abbvie, Amgen, Astellas, Astra Zeneca, Baxalta, Bayer, Biogen, Bristol-Myers Squibb, Celgene, Chiesi, Eisai, Fresenius, Gilead, GSK, Ipsen, Janssen, Leo Pharma, Lilly, MSD, Merck-Serono, Novartis, Pfizer, Roche, Sanofi, Shire, Theramex, UCB, and ViiV for his participation in education, training, and research projects. Miguel Ángel Rodríguez Sagrado has been remunerated for activities for Abbvie, Advanz, Astellas, Amgen, Astra Zeneca, Biogen, Boehringer Ingelheim, Galapagos, Gilead, GSK, Intercept, Janssen, Leo Pharma, Lundbeck, MerckSerono, MSD, Novartis, Roche, Sandoz, Serono, Tesaro, UCB, Vertex and ViiV. The sponsors have not influenced, other than formal aspects, the design and communication of the scientific results and talks. Pere Ventayol has received funding for medical training, giving presentations, and conducting basic research from the following pharmaceutical companies: Sanofi-Genzyme, Janssen, Gilead, Kern, Teva, and Boehringer Ingelheim.

Acknowledgments

The authors would like to thank María Fontanals and Jordi Puig (Ampersand Consulting, Barcelona) for project coordination and methodological support, and Fernando Rico-Villademoros (COCIENTE S.L., Madrid) for editorial assistance. This support was funded by Boehringer Ingelheim España.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.farma.2023.09.004>.

References

- Johansson KA, Chaudhuri N, Adegunsoye A, Wolters PJ. Treatment of fibrotic interstitial lung disease: current approaches and future directions. *Lancet*. 2021;398:1450–60. doi: [10.1016/S0140-6736\(21\)01826-2](https://doi.org/10.1016/S0140-6736(21)01826-2).
- Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. *N Engl J Med*. 2018;378:1811–23. doi: [10.1056/NEJMra1705751](https://doi.org/10.1056/NEJMra1705751).
- Wijnsbeek M, Cottin V. Spectrum of fibrotic lung diseases. *N Engl J Med*. 2020;383:958–68. doi: [10.1056/NEJMra2005230](https://doi.org/10.1056/NEJMra2005230).
- Xaubet A, Ancochea J, Molina-Molina M. Idiopathic pulmonary fibrosis. *Med Clin (Barc)*. 2017;148:170–5. doi: [10.1016/j.medcli.2016.11.004](https://doi.org/10.1016/j.medcli.2016.11.004).
- Xaubet A, Molina-Molina M, Acosta O, Bollo E, Castillo D, Fernández-Fabrellas E, et al. Guidelines for the medical treatment of idiopathic pulmonary fibrosis. *Arch Bronconeumol*. 2017;53:263–9. doi: [10.1016/j.arbres.2016.12.011](https://doi.org/10.1016/j.arbres.2016.12.011).
- Raghu G, Remy-Jardin M, Richeldi L, Thomson CC, Inoue Y, Johkoh T, et al. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults: an official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med*. 2022;205:e18–47. doi: [10.1164/rccm.202202-0399ST](https://doi.org/10.1164/rccm.202202-0399ST).
- Ley B, Collard HR, Talmadge E, King J. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2011;183:431–40. doi: [10.1164/rccm.201006-0894CI](https://doi.org/10.1164/rccm.201006-0894CI).
- Organización Nacional de Trasplantes. Actividad de donación y trasplante pulmonar en España 2021. [citado 3/2/2023]. Available from: <http://www.ont.es/infesp/Memorias/ACTIVIDAD%20DE%20DONACION%20C3%93N%20Y%20TRASPLANTE%20PULMONAR%20ESPA%C3%91A%202021.pdf>.
- Bonella F, Wijnsbeek M, Molina-Molina M, Duck A, Mele R, Geissler K, et al. European IPF Patient Charter: unmet needs and a call to action for healthcare policy-makers. *Eur Respir J*. 2016;47:597–606. doi: [10.1183/13993003.01204-2015](https://doi.org/10.1183/13993003.01204-2015).
- World Health Organization. Noncommunicable Diseases and Mental Health Cluster. Innovative care for chronic conditions: building blocks for actions: global report. World Health Organization; 2002 [citado 3/2/2023]. Available from: <https://apps.who.int/iris/handle/10665/42500>.
- Morrow LE, Hilleman D, Malesker MA. Management of patients with fibrosing interstitial lung diseases. *Am J Health Syst Pharm*. 2022;79:129–39. doi: [10.1093/ajhp/zxab375](https://doi.org/10.1093/ajhp/zxab375).
- Naqvi M, West A. Diagnosis and management of idiopathic pulmonary fibrosis. *Clin Pharm, CP*. 2019;11 doi: [10.1211/CP.2019.20206233](https://doi.org/10.1211/CP.2019.20206233).
- Terrie YC. A review of the treatment and management of idiopathic pulmonary fibrosis. *US Pharm*. 2021;46:HS-8–12.
- Satsuma Y, Ikesue H, Kusuda K, Maeda M, Muroi N, Mori R, et al. Effectiveness of pharmacist-physician collaborative management for patients with idiopathic pulmonary fibrosis receiving pirfenidone. *Front Pharmacol*. 2020;11, 529654. doi: [10.3389/fphar.2020.529654](https://doi.org/10.3389/fphar.2020.529654).
- Sociedad Española de Farmacia Hospitalaria. Plan Estratégico de la Sociedad Española de Farmacia Hospitalaria sobre Atención Farmacéutica al Paciente Crónico. [citado 3/2/2023]. Available from: https://www.sefh.es/sefhpdfs/plan_estrategico_sefh_af_paciente_cronico2012.pdf.
- Morillo-Verdugo R, Calleja-Hernández M, Robustillo-Cortés MLA, Poveda-Andrés JL. A new definition and refocus of pharmaceutical care: the Barbate Document. *Farm Hosp*. 2020;44:158–62. doi: [10.7399/fh.11389](https://doi.org/10.7399/fh.11389).
- Jones J, Hunter D. Consensus methods for medical and health services research. *BMJ*. 1995;311:376–80. doi: [10.1136/bmj.311.7001.376](https://doi.org/10.1136/bmj.311.7001.376).
- Graney BA, He C, Maril M, Matson S, Bianchi P, Cosgrove GP, et al. Essential components of an interstitial lung disease clinic: results from a Delphi survey and patient focus group analysis. *Chest*. 2021;159:1517–30. doi: [10.1016/j.chest.2020.09.256](https://doi.org/10.1016/j.chest.2020.09.256).
- Teoh AKY, Holland AE, Morisset J, Flaherty KR, Wells AU, Walsh SLF, et al. Essential features of an interstitial lung disease multidisciplinary meeting: an international Delphi survey. *Ann Am Thorac Soc*. 2022;19:66–73. doi: [10.1513/AnnalsATS.202011-1421OC](https://doi.org/10.1513/AnnalsATS.202011-1421OC).
- European Medicines Agency. Ofev. Ficha técnica o resumen de las características del producto. [citado 14/2/2023]. Available from: https://www.ema.europa.eu/en/documents/product-information/ofev-epar-product-information_es.pdf.
- Sgalla G, Cerri S, Ferrari R, Ricchieri MP, Poletti S, Ori M, et al. Mindfulness-based stress reduction in patients with interstitial lung diseases: a pilot, single-centre observational study on safety and efficacy. *BMJ Open Respir Res*. 2015;2, e000065. doi: [10.1136/bmjresp-2014-000065](https://doi.org/10.1136/bmjresp-2014-000065).
- Antoniu K, Kamekis A, Symvoulakis EK, Kokosi M, Swigris JJ. Burden of idiopathic pulmonary fibrosis on patients' emotional well being and quality of life: a literature review. *Curr Opin Pulm Med*. 2020;26:457–63. doi: [10.1097/mcp.0000000000000703](https://doi.org/10.1097/mcp.0000000000000703).
- Morillo-Verdugo R, Martínez-Sesmero JM, Lázaro-López A, Sánchez-Rubio J, Navarro-Aznárez H, DeMiguel-Cascón M. Development of a risk stratification model for

- pharmaceutical care in HIV patients. *Farm Hosp.* 2017;41:346–56. doi: [10.7399/fh.2017.41.3.10655](https://doi.org/10.7399/fh.2017.41.3.10655).
24. Sociedad Española de Farmacia Hospitalaria. Modelo de Estratificación y Atención Farmacéutica para pacientes con enfermedades inflamatorias inmunomediadas. [citado 14/2/2023]. Available from: <https://www.sefh.es/mapex/images/Modelo-de-Estratificacion-y-Atencion-Farmaceutica-pacientes-enf-inmunomediadas.pdf>.
 25. Morillo Verdugo R, Garin Escrivà N (coordinadores). Adaptación del Modelo de Atención Farmacéutica CMO al Paciente con Patologías Respiratorias. [citado 29/5/2023]. Available from: <https://www.sefh.es/mapex/images/modelo-CMO-al-paciente-con-patologias-respiratorias.pdf>.
 26. Aronson KI, Danoff SK, Russell AM, Ryerson CJ, Suzuki A, Wijsenbeek MS, et al. Patient-centered outcomes research in interstitial lung disease: an official American Thoracic Society research statement. *Am J Respir Crit Care Med.* 2021;204:e3–23. doi: [10.1164/rccm.202105-1193ST](https://doi.org/10.1164/rccm.202105-1193ST).
 27. Alfageme Michavila I, Calleja MA, Ancochea Bermúdez J, Poveda Andrés JL, Aburto Barrenechea M, Rodríguez Portal JA, et al. Itinerario y pautas de seguimiento farmacoterapéutico de la Fibrosis Pulmonar Idiopática. Madrid: Antares Consulting; 2016.
 28. Near AM, Burudpakdee C, Viswanathan S, Kaila S. Effect of a patient support program for idiopathic pulmonary fibrosis patients on medication persistence: a retrospective database analysis. *Adv Ther.* 2021;38:3888–99. doi: [10.1007/s12325-021-01768-w](https://doi.org/10.1007/s12325-021-01768-w).
 29. Bodreau C, Chaaban S, Hobbs S, Platt T. Impact of a clinical pharmacist and specialty pharmacy services on treatment outcomes in an idiopathic pulmonary fibrosis specialty clinic. *Chest.* 2021;160:A1237. doi: [10.1016/j.chest.2021.07.1137](https://doi.org/10.1016/j.chest.2021.07.1137).
 30. Patel AS, Siegert RJ, Brignall K, Gordon P, Steer S, Desai SR, et al. The development and validation of the King's Brief Interstitial Lung Disease (K-BILD) health status questionnaire. *Thorax.* 2012;67:804–10. doi: [10.1136/thoraxjnl-2012-201581](https://doi.org/10.1136/thoraxjnl-2012-201581).
 31. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care.* 1986;24:67–74. doi: [10.1097/00005650-198601000-00007](https://doi.org/10.1097/00005650-198601000-00007).